



**University of
Zurich**^{UZH}

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2017

Ethical and Privacy Aspects of Using Medical Image Data

Grünberg, K ; Jimenez-del-Toro, O ; Jakab, András ; Langs, G ; Fernandez, T S ; Winterstein, M ;
Weber, M ; Krenn, M

DOI: <https://doi.org/10.1007/978-3-319-49644-3>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-142580>

Book Section

Published Version

Originally published at:

Grünberg, K; Jimenez-del-Toro, O; Jakab, András; Langs, G; Fernandez, T S; Winterstein, M; Weber, M; Krenn, M (2017). Ethical and Privacy Aspects of Using Medical Image Data. In: Hanbury, Allan; Müller, Hening; Langs, Georg. Cloud-Based Benchmarking of Medical Image Analysis. Cham, Switzerland: Springer International Publishing, 33-43.

DOI: <https://doi.org/10.1007/978-3-319-49644-3>

Chapter 3

Ethical and Privacy Aspects of Using Medical Image Data

Katharina Grünberg, Andras Jakab, Georg Langs, Tomàs Salas Fernandez, Marianne Winterstein, Marc-André Weber, Markus Krenn and Oscar Jimenez-del-Toro

Abstract This chapter describes the ethical and privacy aspects of using medical data in the context of the VISCERAL project. The project had as main goals the creation of a benchmark for organ segmentation, landmark detection, lesion detection and similar case retrieval. The availability of a large amount of imaging data was extremely important for the project goals, and thus, we present an analysis of the procedures that were followed for getting access to the data from IRB (internal review board) approval to data extraction and usage. This chapter details the requirements stated by medical ethics committees in three partner countries that supplied data. The exact procedure from request to data distribution is explained. The specific requirements of each data provider (each from a different country) are described in detail. The final data collection was made available in anonymized form in the Microsoft Azure cloud with the restriction of having it on servers that are located inside the European Union.

K. Grünberg · M. Winterstein · M.-A. Weber
University of Heidelberg, Heidelberg, Germany
e-mail: katharina.gruenberg@med.uni-heidelberg.de

A. Jakab · G. Langs · M. Krenn
Medical University of Vienna, Vienna, Austria

G. Langs
e-mail: georg.langs@meduniwien.ac.at

T. Salas Fernandez
Agencia D'Informació, Avaluació i Qualitat en Salut, Catalonia (GENCAT), Spain

O. Jimenez-del-Toro (✉)
University of Applied Sciences Western Switzerland (HES-SO), Sierre, Switzerland
e-mail: oscar.jimenez@hevs.ch

3.1 Introduction

The VISCERAL project developed a cloud-based infrastructure for evaluation of analysis and search tasks on large medical image data sets and organized benchmarks to exploit and compare multiple state-of-the-art solutions designed for segmentation, landmark localization and search [1, 2]. The main Benchmarks focused on automatic identification, localization and segmentation of organs in imaging (Anatomy Benchmarks) [3]. Through VISCERAL, different computational algorithms are brought to large medical imaging datasets to support the evaluation of novel tools for the clinical diagnostic image assessment and workflow. VISCERAL resulted in two types of data-bases as an open resource: the Gold Corpus with expert manual annotations and the Silver Corpus with data computed from benchmark participants’ algorithms [4]. This chapter describes the aspects related to ethics, privacy and the legal basis of the data use, and how the project consortium dealt with them during the project. This chapter gives an overview of the common aspects and highlights the aspects depending on

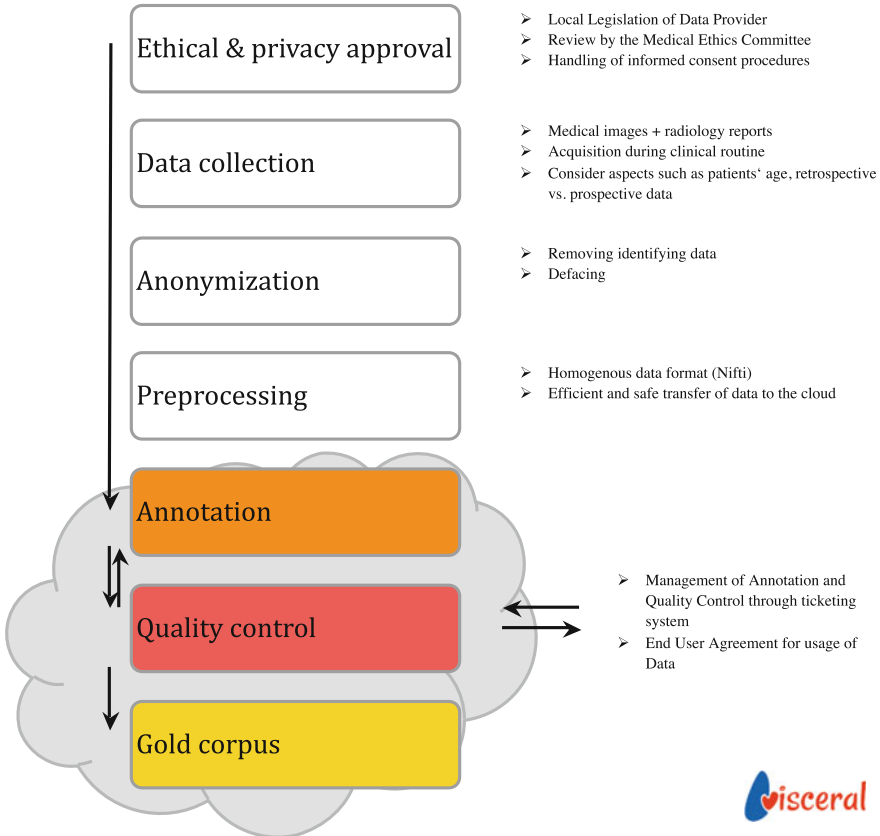


Fig. 3.1 An outline of the steps for data preparation

the country that provided the data. Figure 3.1 shows the data preparation outline to demonstrate the process from getting ethics approval to transferring the data to the cloud platform, where it is harmonized, e.g. transferred to the NIfTI (Neuroimaging Informatics Technology Initiative) format, annotated and quality controlled (see Chap. 4 for a detailed description of the latter steps).

3.2 Ethical and Privacy Aspects for Data Access

The data used in the project consisted of human medical imaging data and their corresponding meta-information. Therefore, its use was subject to specific regulations on both the European Union (EU) and national level that controlled the collection, use, distribution of human data and its inclusion in research studies. There were three data providers in the project:

1. Universitätsklinikum Heidelberg (UKL-HD), Germany
2. Agència d'Informació, Avaluació i Qualitat en Salut (GENCAT), Spain
3. Medizinische Universität Wien (MUW), Austria

Each data provider was responsible for handling the ethical, legal and privacy aspects relevant to the data provided by their group. This typically involves the following:

1. Review of the data collection plan by the local competent medical ethics committee (MEC) / institutional review board (IRB).
2. Handling of informed consent procedures.
3. Anonymization of the data prior to any use or distribution.

Relevant points from these procedures are addressed in more detail in the following sections.

3.2.1 Review by the Medical Ethics Committee

When applying for ethical approval from the competent local/national Ethics Committees, detailed information is provided regarding the following:

- The procedures that are used for the recruitment of participants (e.g. number of participants, inclusion/exclusion criteria, direct/indirect incentives for participation, and the risks and benefits for the participants).
- The nature of the material that will be collected (e.g. imaging data or additional structure data or free text reports).
- It must be explicitly stated if children or adults unable to give informed consent will be involved and, if so, justification for their participation must be provided.
- Detailed information on the informed consent procedures that are implemented.

Before the inclusion of data into the study, the review by the competent local MEC has to be concluded, and the study plan has to be approved by the MEC.

3.2.2 Handling of Informed Consent Procedures

Free informed consent by participants in a medical study is a prime aspect of the ethical considerations concerning medical research. The Declaration of Helsinki states that: “*The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data*”, and “*After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject’s freely-given informed consent, preferably in writing.*” [5]. More detailed discussions are given in [6, 7]. To fulfil the requirements of free informed consent, a participant has to have the right:

- to know that participation is voluntary;
- to ask questions and receive understandable answers before making a decision;
- to know the degree of risk and burden involved in participation;
- to know who will benefit from participation;
- to know the procedures that are implemented in the case of incidental findings;
- to receive assurance that appropriate insurance cover is in place;
- to withdraw themselves, their samples and data from the project at any time;
- to know how their biological samples and data are collected, protected during the project and destroyed at the end; and
- to know of any potential commercial exploitation of the research.

In the context of *retrospective studies* using data acquired prior to study start, and where the collection of informed consent is not feasible or possible, benefits and risks have to be weighted by the competent MEC. There is a discussion regarding research on biological material in the context of biobanks in Tassé et al. [8]. The authors note “*If it is not possible to recontact participants for recontact, some guidelines allow for waived consent for the use of biological material, if certain conditions are met* [9]. However, these conditions are not harmonized among international guidelines.” The authors conclude further “*As stated in the Declaration of Helsinki, ethical principles apply to ‘medical research involving human subjects, including research on identifiable human material or identifiable data’.* It follows that research using anonymised or anonymous data does not create an obligation to obtain informed consent, as the study does not involve identifiable individuals”, taking [5, 10] into account. In [10] the relevant paragraphs emphasize the role of the local competent MEC in the decision of whether consent or recontact is necessary if anonymized data are used:

- “*11. Under certain conditions, personal health information may be included in a database without consent, for example where this conforms with applicable national law that conforms to the requirements of this statement, or where ethical approval was given by a specifically appointed ethical review committee. In these exceptional cases, patients should be informed about the potential uses of their information, even if they have no right to object.*”

- *“14. Approval from a specifically appointed ethical review committee must be obtained for all research using patient data, including for new research not envisaged at the time the data were collected. An important consideration for the committee in such cases is whether patients need to be contacted to obtain consent, or whether it is acceptable to use the information for the new purpose without returning to the patient for further consent. The committee’s decisions must be in accordance with applicable national law and conform to the requirements of this statement.”*

VISCERAL involved the analysis of very large datasets of previously acquired and anonymized data, i.e. of already acquired datasets so that the above-mentioned problems for retrospective studies apply to the VISCERAL project. No additional procedures were conducted linked to the VISCERAL study, and all data were fully anonymized. The decision regarding the requirement of free informed consent procedures was dealt with by each local MEC, according to the relevant legislation.

3.2.3 Anonymization

All data used in the benchmarks are anonymized. Radiology reports were anonymized by removing all patient names, physician names, hospital and institution names and other identifying information. Radiology images were anonymized by blurring face regions in images/volumes that include this body area, removing any embedded text in the image, and locating and removing other identifying information such as serial numbers on implants.

3.2.4 Data Distribution During and After the Benchmarks

All medical data are sensitive by nature. In the context of VISCERAL, it is assured that all data are only available for non-commercial research use and only after signature of a user agreement that assures the use of the data in its given environment and for its research purpose. In VISCERAL, only registered participants can access the data and local copies of the data need to be destroyed after their use for research. The clauses of three ethics committees in Vienna, Barcelona and Heidelberg were taken into account to assure that data treatment is in line with all ethical guidelines. In VISCERAL, only anonymized data are shared in any case and thus all necessary steps are taken into account to assure privacy. The benchmarking campaigns are run in the cloud, in our case the cloud of Microsoft, called Azure (See also Chap. 2). Participants obtain a virtual machine and access to a data source after signing the user agreement with detailed user conditions and rules. All accesses to the virtual machines can be logged as can accesses to the data. Participants in the benchmark have access only

to a small, manually controlled anonymous dataset. Very small subsets can also be made available for download in connection with the user agreement to get used to the data format and image types. The large test dataset, where the anonymization is less carefully controlled, is only accessible by the organizers. Clouds allow for storage of data in chosen geographical regions such as in Europe. This allows making sure that local storage and access rules can be verified and correspond to European legislation.

3.3 Relevant Legislation

All work on data collection of humans is conducted under the rules and legislation in place within the respective countries of the partners, which are based on the following:

- the Declaration of Helsinki (Informed consent for participation of human subjects in medical and scientific research, 2004) and the IHC (International conference on harmonization of technical requirements of pharmaceuticals for human use, Guideline for Good Clinical Practice (1996),
- European Directive 2001/20/EC (April 4, 2001) on Good Clinical Practice for clinical trials,
- Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 (amended 2003) on the protection of individuals with regard to the processing of personal data and on the free movement of such data,
- Regulation (CE) No 45/2001 of the European Parliament and of the Council of 18 December 2001, on the protection of individuals with regard to the processing of personal data by the institutions and bodies of the community and on the free movement of such data.

Furthermore, the Opinions of the European Group on Ethics in Science and New technologies (EGE) (specifically Opinion Nr.13 30/07/1999—Ethical issues of healthcare in the information society) are taken into account.

3.4 Procedures Implemented by Data Providers

Every partner who is data provider (GENCAT, MUW, and UKL-HD) is responsible for the compliance regarding the data contributed by this partner and informs for approval the local medical ethics committee (MEC)/institutional review board (IRB). These committees operate in accordance with international ethical guidelines and the national laws on medical research and protection of the human rights of subjects and privacy.

3.4.1 Agencia D'Informació, Avaluació i Qualitat en Salut, Spain

3.4.1.1 Requirements

Imaging data provided by the Agency to the VISCERAL project are a subset of an electronic health record, “Registre d’informació sanitària de pacients” (Record of patient health information). Patient care is one of the reasons that allow recollection of personal health data, according to data protection laws. Additionally, the health record was declared by the Catalan Health Department to the data protection authority (Declaration to the Data Protection Agency of Catalunya of the file “Registre d’informació sanitària de pacients”, Record of patient health information). Research activities are included among the planned health record usage, and data may be submitted to research groups in the manner provided by the applicable laws. The main laws to be considered in order to transfer personal health information for research projects are as follows:

- ORGANIC LAW 15/1999 of 13 December on the Protection of Personal Data,
- Llei 21/2000, de 29 de desembre, sobre els drets d’informació concernent la salut i l’autonomia del pacient, i la documentació clínica (Patient’s rights and clinical records), and
- LEY 14/2007, de 3 de julio, de Investigación biomédica (Biomedical Research).

According to these laws, in the absence of informed consent from patients, data may be submitted provided that it is effectively anonymized. If obtaining informed consent is not feasible, imaging data can be delivered after an anonymization process.

3.4.1.2 Final Status

The data transfer request was processed by the Department of Health in order to review the legal and ethical questions. No difficulties arose as a result of this reviewing process. Considering the amount of information in image files that could identify an individual or make him/her identifiable, a detailed analysis of the requirements for an effective anonymization of this information was carried out.

3.4.2 Medizinische Universität Wien (Austria)

3.4.2.1 Requirements

The Medical University of Vienna (MUW) provides anonymized medical imaging data to the project. As a general regulation, any study that involves human data

such as VISCERAL conducted at MUW has to be approved by the medical ethics committee (Ethikkommission der Medizinischen Universität Wien,¹ EKMUW).

3.4.2.2 Final Status

At this point, EKMUW has approved the retrospective collection and the publication of anonymized medical imaging data in the course of the VISCERAL project and the involved evaluation. The basis for this decision was a study protocol providing detailed information regarding the study, the anonymization, the assurance of privacy and the data handling. The study protocol was an amendment to an existing protocol that covered the use of anonymized medical imaging data in the KHRESMOI project (Study protocol EK Nr.804/2010-Amendment December 2012). The amendment adds the collection of radiology report data and the publication of anonymized data for evaluation campaign purposes.

3.4.3 *Universitätsklinikum Heidelberg (Germany)*

3.4.3.1 Requirements

The Medical University of Heidelberg (UKL-HD) provides anonymized medical imaging data and corresponding reports to the project. As a general regulation, a study conducted at the UKL-HD has to be approved by the local ethics board (Ethikkommission der medizinischen Fakultät der Universität Heidelberg,² EKUKL-HD). The study must be conducted in accordance with Baden-Württemberg's Medical Association's professional code of conduct (Berufsordnung für Ärztinnen und Ärzte der Landesärztekammer Baden-Württemberg) in its current version. Patient names and all other confidential information are subject to the medical professional secrecy and the provisions of the Federal Data Privacy Act (Bundesdatenschutzgesetzes (BDSG)). A transfer of patient data happens only in anonymized form. Third persons get no insight into the original patient documents.

3.4.3.2 Final Status

The EKUKL-HD was consulted, and a study plan and an ethics proposal were reviewed. The retrospective collection and publication of anonymized medical imaging data in the course of the VISCERAL project and the involved evaluation are accepted under the following conditions:

¹<http://ethikkommission.meduniwien.ac.at/>.

²<http://www.medizinische-fakultaet-hd.uni-heidelberg.de/Ethikkommission.106025.0.html>.

- Only datasets of patient of the age 18 or older are used.
- Retrospective datasets used are of the years 2005–2008, and an informed consent of these patients is not needed, because a retrospective obtention of informed consent would be extremely complex and elaborated without being certainly successful: probably, many patients are already deceased or cannot be contacted.
- In order to maintain further prospective datasets, medical imaging data collected during the clinical routine can be used only of patients (>18 years) that signed an informed consent to agree with the use of their images for the VISCERAL project.

The basis for the decision of the EKUKL-HD is the positive approval of the EKMUW, including a study protocol providing detailed information regarding the study, the anonymization, the assurance of privacy and the data handling, as well as a study protocol that covered the use of anonymized medical imaging data in the KHRESMOI project (Study protocol EK Nr.804/2010-Amendment December 2012).

3.5 Aspects, Recommendations and Conditions for Obtaining Approval from Ethical Committees

Out of the experience with the process of applying for an approval of the ethical boards of the UKL-HD and MUW, we gathered several aspects and recommendations that may help in similar future projects to deal with privacy questions and obtaining approval from ethical committees:

- **Age of patients included:** It may be helpful to only include datasets of patients of the age 18 or older.
- **Usage of retrospective versus prospective datasets:** In Germany, an informed consent by patients is needed. This means to contact every patient by telephone and/or by letter. In Heidelberg, there was the problem that we planned to use retrospective older datasets and that a retrospective obtention of informed consent was extremely complex and elaborated without being certainly successful, since it was probable that many patients were already deceased or moved because of the fact that the image data were out of a sample of patients being severely ill (cancer). Because of this, we obtained the approval to use retrospective older datasets (2005–2009) without informed consent of patients. Usage of prospective or current datasets is only permitted if an informed consent is signed, agreeing with the usage of the patient images and anonymized data for the project.
- **Anonymization of all data:** All selected image datasets were anonymized individually and locally by the three data providers. For anonymization, the following items were removed from the DICOM headers: date of birth (only age was preserved), institution name, patient name, patient ID, examination number and study date. A key of the patient ID and the referring pseudonym is held by the data provider and stored individually. Other metadata, such as clinical questions

and radiology reports, were anonymized, using only extracted RadLex terms (and their negations) from the reports. Additionally, whole-body CT scans were defaced (image data of the face were partly blurred), in order to ensure that no identification of a patient is possible.

- **End-User Agreement:** In order to ensure the correct and only scientific usage of the data, benchmark participants have to sign an end-user agreement. The signed agreements were checked and approved individually by Benchmark organizers.
- **Safe storage in the cloud:** VISCERAL Benchmarks are run on cloud servers, provided by Microsoft (Azure). Only authorized participants who signed the end-user agreements have access to the stored data. The data access closes when a benchmark is finished. Participants only have access to a small, well-chosen and anonymized dataset for training their algorithms. Since the cloud servers had to be in Europe, they are subject to European law. Access regulation and local data storage are secure and protected by European law.
- **Long-term usage of data:** A central element of sustainable, deep-impacting evaluation campaigns in developing new methods is the long-term availability of the data. VISCERAL aims at providing the data over a long period of time. Comparable datasets are the BRATS dataset for computer-based segmentation of brain lesions.³ A deletion of the data after the end of the project would mean that the results of VISCERAL are not reproducible and can no longer be verified. In order to maintain the results and the scientific progress achieved through the project, the EKUKL-HD agreed to provide the data three more years after the end of the project. If further usage of the data is needed, an additional amendment for the corresponding study protocol will be provided.

3.6 Conclusion

Acquiring medical imaging research data in multicentre studies is not an easy process. All data acquisition requires that data privacy be respected and needs to be agreed upon by medical ethics commissions of the participating institutions. This chapter describes the steps that were taken in the VISCERAL project and some lessons learned to avoid delays in data acquisition that can also be useful for similar future projects. Safe storage and access of data in the cloud has a promising future for medical data analysis, as the risks of data misuse can be reduced in a straightforward way.

Acknowledgements The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007–2013) under grant agreement 318068 (VISCERAL).

³<http://www2.imm.dtu.dk/projects/BRATS2012>, <https://vsd.unibe.ch/WebSite/BRATS2012/Start>.

References

1. Hanbury A, Müller H, Langs G, Weber MA, Menze BH, Fernandez TS (2012) Bringing the algorithms to the data: cloud-based benchmarking for medical image analysis. In: Catarci T, Forner P, Hiemstra D, Peñas A, Santucci G (eds) CLEF 2012. LNCS, vol 7488. Springer, Heidelberg, pp 24–29. doi:[10.1007/978-3-642-33247-0_3](https://doi.org/10.1007/978-3-642-33247-0_3)
2. Langs G, Hanbury A, Menze B, Müller H (2013) VISCERAL: towards large data in medical imaging — challenges and directions. In: Greenspan H, Müller H, Syeda-Mahmood T (eds) MCBR-CDS 2012. LNCS, vol 7723. Springer, Heidelberg, pp 92–98. doi:[10.1007/978-3-642-36678-9_9](https://doi.org/10.1007/978-3-642-36678-9_9)
3. Jiménez-del Toro OA, Müller H, Krenn M, Gruenberg K, Taha AA, Winterstein M, Eggel I, Foncubierta-Rodríguez A, Goksel O, Jakab A, Kontokotsios G, Langs G, Menze B, Salas Fernandez T, Schaer R, Walleyo A, Weber MA, Dicente Cid Y, Gass T, Heinrich M, Jia F, Kahl F, Kechichian R, Mai D, Spanier AB, Vincent G, Wang C, Wyeth D, Hanbury A (2016) Cloud-based evaluation of anatomical structure segmentation and landmark detection algorithms: visceral anatomy benchmarks. *IEEE Trans Med Imaging* 35(11):2459
4. Krenn M, Dorfer M, Jiménez del Toro OA, Müller H, Menze B, Weber MA, Hanbury A, Langs G (2016) Creating a large-scale silver corpus from multiple algorithmic segmentations. In: Menze B, Langs G, Montillo A, Kelm M, Müller H, Zhang S, Cai W, Metaxas D (eds) MCV 2015. LNCS, vol 9601. Springer, Cham, pp 103–115. doi:[10.1007/978-3-319-42016-5_10](https://doi.org/10.1007/978-3-319-42016-5_10)
5. World Medical Association Declaration of Helsinki (2001) Ethical principles for medical research involving human subjects. *Bull World Health Organ* 79(4):373
6. Elger B, Iavindrasana J, Lo Iacono L, Müller H, Roduit N, Summers P, Wright J (2010) Strategies for health data exchange for secondary, cross-institutional clinical research. *Comput Methods Programs Biomed* 99(3):230–251
7. Hughes J, Hunter D, Sheehan M, Wilkinson S, Wrigley A (2010) European textbook on ethics in research. Publications Office of the European Union, Luxembourg
8. Tassé AM, Budin-Ljøsne I, Knoppers BM, Harris JR (2010) Retrospective access to data: the ENGAGE consent experience. *Eur J Hum Genet* 18(7):741–745
9. Vayena E, Ganguli-Mitra A, Biller-Andomo N (2013) Guidelines on biobanks: emerging. Ethical issues in governing biobanks: global perspectives. Ashgate Publishing, Farnham, pp 23–35
10. Declaration on ethical considerations regarding health databases (2002) WMA General Assembly, Washington (s 1)

Open Access This chapter is licensed under the terms of the Creative Commons Attribution- Non-Commercial 2.5 International License (<http://creativecommons.org/licenses/by-nc/2.5/>), which permits any noncommercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

